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09/719,272	05/04/2001	Hiroshi Yamamoto	19036/36959	7004

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EXAMINER	
YU, MISOOK	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 03/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/719,272	YAMAMOTO ET AL.	
	Examiner	Art Unit	
	MISOOK YU, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,4,6-19 and 28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) *11 and 14* is/are allowed.

6)☒ Claim(s) *3, 4, 6-10, 12, 13, 15-19, and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 9/8/2003
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 3, 4, 6-13, 15-19, and 28 are amended. Claims 3, 4, 6-19, and 28 are pending and under consideration.

This Office action contains new grounds of rejection.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Claim Rejections - 35 USC § 112, Withdrawn

The rejection of claims 12 and 13 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the amendment.

Claim Rejections - 35 USC § 102, Withdrawn

The rejection of claims under 35 U.S.C. 102(b) as being anticipated by Streuli et al (1992, The EMBO Journal, vol. 11, pages 897-907) is withdrawn because the Office no longer interprets the amended claims as drawn to monoclonal antibody to any epitope in the 1897 amino acids LAR.

The rejection of claims under 35 U.S.C. **102(b)** as being anticipated by Takeuchi et al (1993, IDS filed on 5/3/2001 #C9, Tissue Antigens 42; 441) as evidenced by Streuli et al (cited above) is withdrawn because applicant's argument is persuasive in that the antibody of record binds to both LAR and CD45.

The rejection of the claims under 35 U.S.C. **102(b)** as being anticipated by either Ahmad et al (1995, J Clin Invest; 95 :2806-12) or Ahmad et al (1997, J. Biol. Chem. vol. 272, pages 448-457) is withdrawn because the amended claims are now drawn to making monoclonal antibodies.

Claim Rejections - 35 USC § 103, Maintained

Claims 1-4, 6-10, 12, 13, 15-19, and 27 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Ahmed (1997, J. Biol. Chem. vol. 272, pages 448-457) or Ahmed (1995, J Clin Invest; 95 :2806-12), and further in view of Streuli et al (1992, cited above).

The amended claims are interpreted as drawn to monoclonal anti-LAR antibody capable of binding a cytosolic domain of LAR phosphate subunit but incapable of CD45 or hybridoma producing said antibody.

Applicant argues that none of the cited references alone or in combination teach or suggest a monoclonal antibody that binds to the intracellular domain of a LAR P-subunit, wherein the antibody fails to cross-react with CD45; the Office fails to state a use for monoclonal antibodies immunoreactive with the intracellular domain of the LAR P subunit, but fails to cross-react with CD45; a role of the LAR P subunit in obesity and diabetes does not in and of itself provide a motivation for producing the claimed antibodies; the Office also failed to state the likelihood of success of producing the claimed antibodies of instant application that has unexpected properties (i.e. specifically recognize cancerous thyroid cells distinct from normal thyroid cells. These arguments have been fully considered but found unpersuasive.

As for unexpected result argument, the argument is not commensurate in scope of the claims because the claims are not limited to the unexpected antibodies, but broadly drawn to any monoclonal antibody capable of binding a cytosolic domain of LAR phosphate subunit but incapable of CD45. Further, it appears that the unexpected properties (i.e. specifically recognize cancerous thyroid cells distinct from normal thyroid cells) are not due to the inherent properties of the claimed invention but due to characteristics of normal thyroid cells vs. cancerous thyroid cells i.e. cancerous thyroid cells express a cytosolic domain of LAR phosphate subunit but normal thyroid cells do not expresses a cytosolic domain of LAR phosphate subunit. In other words, the unexpected result appears that cancerous thyroid cells express a cytosolic domain of LAR phosphate subunit while normal thyroid cells do not express said subunit.

In response to applicant's argument that the cited references alone or in combination teach or suggest a monoclonal antibody that binds to the intracellular domain of a LAR P-subunit, wherein the antibody fails to cross-react with CD45, the Office reiterates that combination of the primary references and the secondary reference teach or suggest the claimed invention and also teach all the necessary technical steps to arrive at the instant invention with a reasonable expectation of success because the primary references teach a domain of LAR that has a phosphatease activity is important for an important human disease (i.e. diabetes); this teaching gives motivation to make and use antibody specific for domain of LAR that has phosphatase activity. The primary references do not teach where a domain of LAR with a phosphatease activity is located. However, Streuli et al at Fig. 3 teach that most of

the primary amino acid sequences of LAR **P**- subunit (i.e. **p**hosphatase subunit) lies inside membrane (cytosole) Further Streuli et al at page 906 teach the all the necessary method of how to make hybridoma producing only monoclonal antibody and also teaches method to screen antibodies capable of binding only one protein (i.e. LAR) but does not cross-react with the structurally related protein (i.e. CD45). Further Bendayan (C15 of the IDS filed on 09/11/2003) teaches that monoclonal antibodies cross-react with other similar sequences are the main culprit giving false immunocytochemical results, which could muck up the experimental results.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to make and use the monoclonal antibody capable of binding to only one of the intended domain of protein (LAR) important for a human diabetes with reasonable expectation of success given the high levels of skill in the art. The Board of Patent Appeals and interferences has taken the position that once an antigen has been isolated, the manufacture of antibodies against it is *prima facie* obvious. See Ex parte Erlich 22 USPQ2d 1463 (BdPatApp&Int 1992). One would be motivated to make and use instantly claimed antibody for immuochemistry work before one can conclude that the result comes from neutralizing only LAR phosphase activity, not neutralizing phosphase activity of CD45, thereby eliminating the criticism of peers saying "the result came from cross-reacting antibody to CD45".

Double Patenting, Withdrawn

The rejection of claims rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, and 5-21 of

copending Application No. 09/719,272 is withdrawn because all the claims in copending Application No. 09/719,272 are drawn to monoclonal antibody capable of binding to both LAR and CD45.

NEW GROUNDS OF REJECTION

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 28 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 28 recite "the antibody's **specific** immunoactivity to LAR distinguishes thyroid carcinoma cells from normal thyroid cells" but it is not clear what the metes and bounds are. The specification at Figures 11-13 teaches that a different expression pattern of LAR between normal thyroid cells and cancerous thyroid cells distinguishes thyroid carcinoma from normal thyroid cells. The specification does not teach any special or subgroups of monoclonal anti-LAR antibody of the base claim 3 have recited characteristics i.e. a **specific** immunoactivity to LAR distinguishes thyroid carcinoma cells from normal thyroid cells.

Claims 3, 4, 6-10, 12, 13, 15-19, and 20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is new matter rejection. The amended claims 3, 15, 16, 19, have new limitations "specifically immunoreacts with" and "does not cross-react with". Applicant states that support for the new limitations are found at page 41 lines 24-26, where it says that "In this ELISA method, hybridoma was selected, which did not show any immune response to the wells bound with GST or GST-CD45, but showed an immune response only to the wells bound with GST-LAR". The line bridging page 6 and 7 says that the invention is to develop antibody specific to intracellular domain of LAR, not CD45. The original claims say "antibody having specificity to intracellular domain of LAR and having no specificity to CD45". However, the specification as originally filed does not have support for the newly presented limitations. Is "having no specificity" same as "does not cross-react"? Is "having specificity" same as "specifically immunoreacts with"?

Claims 8 and 17-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is new matter rejection. This rejection is due to the new limitation "about". Applicant states that the support is found at page 38, line 24, where it say that cell culture were incubated at 25 ^{o}C overnight. However, the specification as originally filed does not say "about 20-30" or "about 16-24 hours".

applicant is requested to point support in the specification as originally filed since the Office is unable to find such support.

Claim 28 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 28 as currently construed say that the antibody's **specific** immunoactivity to LAR distinguish thyroid carcinoma cells from normal thyroid cells. However, the specification as originally filed does not discloses any such antibody. The Office is not able to find a support for the newly added limitation, therefore applicant is requested to point out the support in the specification as originally filed.

Allowable Subject Matter

Claims 11, and 14 are allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on 09/08/2003 prompted the new

ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 609(B)(2)(i). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 571-272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne C Eyler can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MISOOK YU, Ph.D.
Examiner
Art Unit 1642

LARRY R. HELMS, PH.D
PRIMARY EXAMINER